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Pulmonary function in premature infants
Rupture of the amniotic membranes

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Recent studies in animals have suggested that antenatally administered steroids may accelerate fetal lung maturation and prevent the development of respiratory distress following premature delivery [7, 13, 16, 18, 21, 23]. Further studies in human pregnancies complicated by premature rupture of the amniotic membranes [1, 3, 4, 19, 24], intrauterine growth retardation [6], or maternal heroin addiction [22] have all been consistent with the hypothesis that an intrauterine stress may promote secretion of cortisone by either the mother or fetus and hasten the development of pulmonary surfactant, thereby reducing the incidence of hyaline membrane disease. Such stresses are not without risks to the fetus. In particular, the fetus exposed to the risk of prolonged rupture of the amniotic membranes is an increasing risk of infection as the time between rupture of the amniotic membranes and delivery lengthens [11, 20]. In such cases the perinatologist must weigh and balance the risks of prematurity, hyaline membrane disease, and infection against the possible benefits of increased maturity at birth, particularly in terms of pulmonary function. The purpose of the present investigation was to apply standard techniques of pulmonary function testing to a group of premature infants to determine whether or not prolonged rupture of the membranes had any significant effect on pulmonary function.

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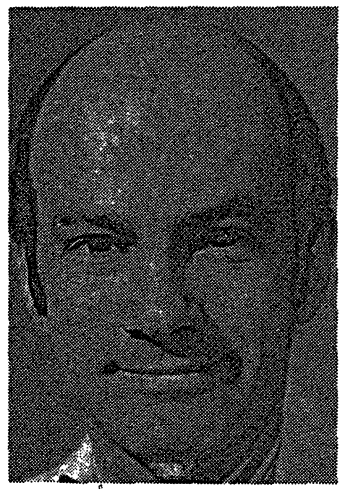
Curriculum vitae



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1 Methods

A total of 26 infants was included in the present study. No infant in the present study demonstrated clinical or radiographic evidence of hyaline membrane disease on admission to the Neonatal Intensive Care Unit. All were studied at 24 hours of age and again at 7 days of age. All were of appropriate weight for gestational age, as determined from standard physical criteria [9], obstetrical history, and charts of intrauterine growth [2]. The infants were further divided into two groups on the basis of an obstetrical history of rupture of the amniotic membranes before delivery. Infants considered to have been born following prolonged rupture of the maternal membranes were all

delivered to women whose membranes had been ruptured by the standard clinical criteria of pH testing of vaginal fluid, history, and physical examination. Rupture in all cases took place at least 18 hours prior to delivery. In the group without prolonged rupture of the membranes, membranes were either intact at delivery or ruptured during labor. This duration was less than 12 hours in all cases. The average duration of rupture of the amniotic membranes in the group of infants under 1500 grams was 115 hours, with a standard deviation of 77 hours and a range of 48 to 288 hours. In the larger infants, the average duration was 68 hours, with a standard deviation of 62 hours and a range of 19 to 336 hours. This difference is not statistically significant ($t = 2.00$, $p > 0.05$). One mother in each group developed febrile illnesses before delivery attributed to amnionitis. All mothers were in labor at the time of delivery, although three mothers (one of an infant under 1500 grams, two of larger infants) required cesarean section. The infants were further divided into two groups according to birth weight at 1500 grams (approximately 32 weeks in gestational age). This division was made on the basis of data suggesting steroids administered to the mother after this period have the greatest effect on pulmonary maturity [17]. Further data on these infants is presented in Tabs. I and II.

Arterial blood was drawn from either a temporal or right radial artery while the infant was breathing room air and resting quietly in an incubator maintained at the infant's thermoneutral temperature. Arterial oxygen tension (PaO_2), arterial carbon dioxide tension ($PaCO_2$) and arterial pH were immediately determined on an Instrumentation Laboratories 123 ultramicro system calibrated with gas and blood. Functional residual capacity (FRC) was determined by helium dilution [14]. Pulmonary compliance was determined by means of a water-filled intraesophageal catheter attached to a manometrically calibrated Statham strain gauge, for recording intrathoracic pressure changes, and a MedSciences pediatric wedge spirometer calibrated

Tab. I. Data on infants weighing less than 1500 grams at birth

	No premature rupture of amniotic membranes			Premature rupture of membranes over 18 hours				
Day 1	*n*	*Mean ± 1 S.D.*	*Range*	*n*	*Mean ± 1 S.D.*	*Range*	*t*	*p*
Birth weight (grams)	10	1123 ± 234	840–1420	6	992 ± 246	850–1420	1.068	N.S.
PaO_2 mm Hg	9	56 ± 12	47–85	6	51 ± 6	44–60	0.908	N.S.
$PaCO_2$ mm Hg	9	35 ± 8	26–45	6	37 ± 7	26–48	0.452	N.S.
pH	9	7.42 ± 0.06	7.35–7.47	6	7.43 ± 0.04	7.38–7.47	0.379	N.S.
FRC (cc)	8	48 ± 12	35–66	6	43 ± 19	22–70	0.552	N.S.
FRC (cc/cm of body length)	8	1.3 ± 0.3	1.0–1.7	6	1.2 ± 0.5	0.7–1.7	0.516	N.S.
compliance (C_L) cc/cm H_2O	7	1.39 ± 0.80	0.49–2.36	5	1.74 ± 1.28	0.21–3.22	0.590	N.S.
specific C_L (C_L/cc FRC)	5	0.030 ± 0.017	0.012–0.054	5	0.042 ± 0.039	0.010–0.104	0.671	N.S.
Day 7								
PaO_2 mm Hg	5	65 ± 15	52–90	3	60 ± 15	47–76	0.449	N.S.
$PaCO_2$ mm Hg	5	36 ± 4	30–40	3	46 ± 2	44–48	1.202	N.S.
pH	5	7.38 ± 0.05	7.30–7.44	3	7.35 ± 0.03	7.33–7.38	0.846	N.S.
FRC (cc)	7	35 ± 15	14–52	5	25 ± 9	16–38	1.488	N.S.
FRC (cc/cm of body length)	6	1.0 ± 0.4	0.9–1.4	5	0.7 ± 0.2	0.5–1.0	1.672	N.S.
compliance (C_L) cc/cm H_2O	5	2.05 ± 1.19	0.83–3.88	4	1.72 ± 1.17	0.67–2.11	0.417	N.S.
specific C_L (C_L/cc FRC)	4	0.048 ± 0.022	0.020–0.075	4	0.088 ± 0.083	0.022–0.200	0.950	N.S.

Tab. II. Data on infants weighing more than 1500 grams at birth

	No premature rupture of amniotic membranes			Premature rupture of membranes over 18 hours				
	n	*Mean ± 1 S.D.*	*Range*	*n*	*Mean ± 1 S.D.*	*Range*	*t*	*p*
Day 1								
Birth weight (grams)	3	1770 ± 56	1710–1820	8	1847 ± 189	1620–2200	0.679	N.S.
PaO_2 mm Hg	3	53 ± 17	34–65	8	63 ± 10	51–80	1.226	N.S.
$PaCO_2$ mm Hg	3	33 ± 3	29–35	8	31 ± 7	17–38	0.558	N.S.
pH	3	7.43 ± 0.04	7.38 –7.45	8	7.40 ± 0.05	7.32–7.48	0.804	N.S.
FRC (cc)	2	59 ± 6	54–63	7	58 ± 11	43–74	0.008	N.S.
FRC (cc/cm of body length)	2	1.4 ± 0.1	1.3–1.5	5	1.4 ± 0.3	1.0–1.7	0.022	N.S.
compliance (C_L) (cc/cm H_2O)	3	3.60 ± 3.04	1.17–7.01	7	2.20 ± 1.06	0.74–3.52	1.143	N.S.
specific C_L (C_L/FRC)	2	0.086 ± 0.061	0.042–0.130	6	0.035 ±0.014	0.017–0.060	2.283	N.S.
Day 7								
PaO_2 mm Hg	2	65 ± 21	35–37	5	32 ± 5	26–39	1.205	N.S.
pH	2	7.44 ± 0.01	7.43–7.44	5	7.45 ± 0.02	7.42–7.48	1.098	N.S.
FRC (cc)	1	71	–	5	64 ± 1	63–66	–	–
FRC (cc/cm of body length)	1	1.7	–	5	1.5 ± 0.3	0.9–1.7	–	–
compliance (C_L)	1	0.70	–	5	3.72 ± 4.58	0.48–11.77	–	–
specific C_L (C_L/FRC)	1	0.010	–	5	0.058 ± 0.071	0.008–0.184	–	–

electronically and volumetrically, for determination of tidal volume and respiratory flow. These instruments recorded on a four-channel HEWLETT-PACKARD polygraph. Compliance was determined according to the method of COOK [5]. Intraesophageal measurement of pressures results in a systematic error of about 5% when compared with intrapleural pressures [8]. This systematic error would not effect comparisons between groups, or in individuals at differing ages, as in the present study. For purposes of comparison, lung volume was standardized against the patient's body length [14] and expressed as ml. of FRC/centimeter of body length (ml FRC/cm.). Specific compliance (compliance/ml FRC) was also determined. As noted in Tabs. I and II, not all patients underwent a complete set of tests. The number of infants receiving each test is indicated in the tables.

Patients were studied with their parents knowledge and consent. All studies were reported as part of the patient's clinical record and were used for diagnostic and therapeutic purposes.

2 Results

Clinical data on infants weighing less than 1500 grams at birth is presented in Tab. I, and data on larger infants is presented in Tab. II. All infants had normal arterial blood gases when breathing room air when studied at one day and at one week of age. Lung volumes were also within normal limits at both intervals. When infants of similar birth weight were compared at similar ages, no statistically significant differences were found. No significant differences were found when total and specific pulmonary compliance were compared in infants with and without prolonged rupture of the amniotic membranes.

Pulmonary function in larger infants remained essentially unchanged from day 1 when these infants were studied again on day 7. Infants under 1500 grams showed a loss of functional residual capacity associated with a decrease in arterial oxygenation and an increase in arterial carbon dioxide and a small fall in arterial pH.

These changes in small infants took place whether or not amniotic membranes were ruptured for more than 18 hours. The magnitude of this deterioration was greater in infants born after rupture of the amniotic membranes, although this difference was not statistically significant.

In summary, no statistically significant differences in pulmonary function, as measured by arterial gas tensions, lung volumes, and compliance, were found when two groups of premature infants were compared at one and seven days of age whose antenatal histories differed only in the duration of rupture of the amniotic membranes before delivery.

3 Discussion

Previous studies on animals given steroids during late fetal life have demonstrated histologic and functional acceleration of pulmonary function when compared with untreated controls [7, 13, 16, 18, 21, 23]. A similar enhancement of pulmonary function should be apparent in premature human infants born after a stress sufficient to cause endogenous secretion of steroids. The reduced incidence of respiratory distress in infants born following prolonged rupture of the amniotic membranes has been advanced as evidence for such enhancement of pulmonary function [1, 3, 4, 24]. Amniotic fluid lecithin/sphingomyelin ratios have been shown to rise following premature rupture of the membranes, suggesting an improvement in pulmonary function following birth [19]. The results of the present study are consistent with the thesis that pulmonary function in infants born after prolonged rupture of the amniotic membranes is similar to that of healthy, non-distressed premature infants.

Not all published data support this hypothesis, however. A recent large retrospective study, based on clinical material, found no significant reduction in the incidence of respiratory distress following prolonged rupture of the amniotic membranes [12]. FRANTZ and colleagues were unable to demonstrate acceleration of pulmonary function in sheep fetuses following removal of amniotic fluid [10]. Clinical material is heterogeneous, however, and a retrospective study based on chart records [12] may be difficult to carry out in terms of assessment of the severity of respiratory distress. Animal work, by its nature well-controlled, may not be analogous to the situation in human premature rupture of the membranes where infection may play a part in producing the stress needed to enhance pulmonary function. Enhancement of pulmonary function has been found in infants with the stress of dysmaturity [6], and this degree of enhancement was not seen in the premature infants included in the present study. The dysmature infants involved in the previous study had enhanced lung function when compared to premature infants of similar birthweight but lesser maturity. Therefore these earlier results are not inconsistent with the present study which compares nondistressed premature infants of similar weights and maturities.

The effects of prolonged rupture of the amniotic membranes on pulmonary function appear to be confined to the first days after birth. A form of delayed deterioration in lung function in premature infants termed chronic pulmonary insufficiency of prematurity (CPIP) has been described by KRAUSS and colleagues [15] in premature infants under 1300 grams at birth. This syndrome is characterized by a loss in lung volume and is associated with elevations in carbon dioxide tension and falling arterial oxygen tension and pH. These alterations in pulmonary function were also seen in infants weighing less than 1500 grams at birth in the present study. Therefore, while premature rupture of the amniotic membranes may enhance pulmonary function immediately following birth, this complication does not ensure continued adequate pulmonary function in small premature infants.

Summary

Pulmonary function was studied at one and seven days of age in two groups of infants matched for weight and maturity.

All infants tolerated room air at birth and none had physiologic or radiologic evidence of respiratory distress. These infants were subdivided on the basis of a history of antenatal rupture of the amniotic membranes into groups with rupture of the membranes less than 18 hours before delivery and a low birth weight group with an average duration of 115 ± 77 hours of rupture and a more mature

group (over 1500 grams at birth) with an average duration of 68 ± 62 hours of ruptured membranes. Statistical comparison revealed no significant differences in arterial blood gases, arterial pH, functional residual capacity, or compliance between infants with and without an antenatal history of ruptured membranes. All infants had normal pulmonary function according to their maturity, and no enhancement beyond this level was seen in infants with prolonged rupture of the amniotic membranes. These data are consistent with the hypothesis that pulmonary function following prolonged rupture of the amniotic membranes in premature infants is normal.

Keywords: Amniotic membranes, complications in pregnancy, premature infant, pulmonary function, respiratory distress of the newborn.

Zusammenfassung

Die Lungenfunktion bei unreifen Neugeborenen nach Blasensprung

Die Lungenfunktion wurde an ein und sieben Tage alten Neugeborenen geprüft, wobei 2 Untersuchungskollektive hinsichtlich Gewicht und Reifegrad unterschieden wurden.

Alle Kinder tolerierten bei der Geburt Zimmerluft und keines der Neugeborenen zeigte physiologische oder radiologische Anzeichen eines RDS. Diese Neugeborenen wurden je nach Zeitpunkt des antenatalen Blasensprungs in 3 Gruppen unterteilt: in der 1. Gruppe lag der Blasensprung weniger als 18 h vor der Geburt zurück. Die 2. Gruppe bildeten Neugeborene mit einem niedrigen Geburtsgewicht, bei denen der Blasensprung durchschnittlich 115 ± 77 Stunden zurücklag und in einer weiteren Gruppe wurden reifere Kinder (mehr als 1500 g Geburtsgewicht) zusammengefaßt, wobei der Blasensprung im Durchschnitt 68 ± 62 Stunden vor der Geburt erfolgt war.

Der statistische Vergleich ergab keine signifikanten Unterschiede bezüglich der Blutgaswerte, des arteriellen pH-Werte sowie der Residualkapazität zwischen den Gruppen mit verschiedenen Zeitpunkt des antenatalen Blasensprungs. Alle Kinder hatten eine ihrem Reifegrad entsprechende normale Lungenfunktion. Eine verstärkte Symptomatik einer anormalen Lungenfunktion konnte bei Neugeborenen nach vorzeitigem Blasensprung nicht gefunden werden.

Diese Ergebnisse stehen in Einklang mit der Hypothese, daß die Lungenfunktion von unreifen Neugeborenen nach vorzeitigem Blasensprung normal ist.

Schlüsselwörter: Fruchtblase, Lungenfunktion, RDS des Neugeborenen, Schwangerschaftskomplikationen, unreife Neugeborene.

Résumé

Fonction pulmonaire des prématures en cas de rupture des membranes amniotiques

Notre présente étude a porté sur l'observation de la fonction pulmonaire à l'âge de un et de sept jours dans deux groupes de bébés sélectionnés selon le poids et la maturité. Tous les bébés ont supporté l'air ambiant à l'accouchement et aucun n'a manifesté d'asphyxie périnatale sur le plan physiologique et radiologique. Ces bébés ont été subdivisés selon le critère de la rupture des membranes amniotiques avant l'accouchement en groupes avec rupture moins de 18 h. avant l'accouchement et un groupe avec souspoids de naissance et une durée moyenne de 115 ± 77 h. de rupture et un groupe plus mature (plus de 1500 g à la naissance) avec une durée moyenne de 68 ± 62 h. de rupture. Les rapprochements statistiques n'ont montré aucune différence significative dans les gaz du sang artériel, dans le pH artériel, dans la capacité résiduelle fonctionnelle ou dans la conformité entre bébés avec et sans antécédents antenatals de rupture de membranes. Tous les enfants ont eu une fonction pulmonaire normale pour leur maturité et on n'observa aucune hausse au-delà de ce niveau chez les bébés avec rupture prolongée des membranes amniotiques. Ces données confirment l'hypothèse selon laquelle la fonction pulmonaire reste normale chez les prématurés après une rupture prolongée des membranes amniotiques.

Mots-clés: Asphyxie périnatale, bébé prématuré, fonction pulmonaire, grossesse, complications, membranes amniotiques.

Bibliography

[1] ALDEN, E. R., T. MANDELKORN, D. E. WOODRUM, R. P. WENNBERG, C. R. PARKS, W. A. HODSON: Morbidity and mortality of infants weighing less than 1000 grams in an intensive care nursery. Pediatrics 50 (1972) 40

[2] BATTAGLIA, F. C., L. O. LUBCHENCO: A practical classification of newborn infants by weight and gestational age. J. Pediatrics 71 (1967) 159

[3] BAUER, C. R., L. STERN, E. COLLE: Prolonged rupture of the membranes associated with a decreased incidence of respiratory distress syndrome. Pediatrics 53 (1974) 7

[4] CHISWICK, M. L., E. BURNARD: Respiratory distress syndrome (letter). Lancet 1 (1973) 1060

[5] COOK, C. C., J. M. SUTHERLAND, S. SEGAL, R. B. CHERRY, J. MEAD, M. B. MCILROY, C. A.

SMITH: Studies of respiratory mechanics in the newborn infant. III. Measurements of the mechanics of respiration. J. Clin. Invest. 36 (1957) 440
[6] DAHMS, B. B., A. N. KRAUSS, P. A. M. AULD: Pulmonary function in dysmature infants. J. Pediatrics 84 (1974) 434
[7] DELEMOS, R. A., D. W. SHERMETA, J. H. KNELSON: Acceleration of appearance of pulmonary surfactant in the fetal lamb by administration of corticosteroids. Amer. Rev. Resp. Dis. 102 (1970) 459
[8] DINWIDDIE, R., G. RUSSEL: Relationship of intraesophageal pressure to intrapleural pressure in the newborn. J. Appl. Physiol. 33 (1972) 415
[9] DUBOWITZ, L. M. S., V. DUBOWITZ, C. GOLDBERG: Clinical assessment of gestational age in the newborn infant. J. Pediatrics 77 (1970) 1
[10] FRANTZ, I. D., S. M. ADLER, B. T. THACH, I. WYSZOGRODSKI, B. D. FLETCHER, H. W. TAEUSCH, M. E. AVERY: The effect of amniotic fluid removal on pulmonary maturation in sheep. Pediatrics 56 (1975) 474
[11] GUNN, G. C., D. R. MISHELL, D. G. MORTON: Premature rupture of the fetal membranes. Amer. J. Obstet. Gynec. 106 (1970) 469
[12] JONES, M. D., L. I. BURD, W. A. BOWERS, F. C. BATTAGLIA, L. O. LUBCHENCO: Failure of association of premature rupture of the membranes with respiratory distress syndrome. New England J. Medicine 292 (1975) 1253
[13] KOTAS, R. V., M. E. AVERY: Accelerated appearance of pulmonary surfactant in the fetal rabbit. J. Appl. Physiol. 30 (1971) 358
[14] KRAUSS, A. N., P. A. M. AULD: Measurement of functional residual capacity in distressed neonates by helium rebreathing. J. Pediatrics 77 (1969) 228
[15] KRAUSS, A. N., D. B. KLAIN, P. A. M. AULD: Chronic pulmonary insufficiency of prematurity (CPIP). Pediatrics 55 (1975) 55
[16] LIGGINS, G. C.: Premature delivery of foetal lambs infused with glucocorticoids. J. Endocr. 45 (1969) 515
[17] LIGGINS, G. C.: Prevention of RDS by maternal betamethasone administration. In: Proceedings of the Seventieth Ross Conference on Pediatric Research, lung maturation and the prevention of hyaline membrane disease. Ross Laboratories, Columbus, Ohio 1976.
[18] MOTOYAMA, E. K., M. M. ORZALESI, Y. KIKKAWA, M. KAIBARA, B. WU, C. J. ZIGAS, C. D. COOK: Effect of cortisol on the maturation of fetal rabbit lungs. Pediatrics 48 (1971) 547
[19] RICHARDSON, C. J., J. J. POMERANCE, M. D. CONNINGHAM, L. GLUCK: Acceleration of fetal lung maturity following prolonged rupture of the membranes. Amer. J. Obstet. Gynec. 118 (1974) 1115
[20] SHUBECK, F., R. C. BENSON, W. W. CLARK, H. BERENDES, W. WEISS, J. DEUTSCHBERGER: Fetal hazard after rupture of the membranes. Obstet. Gynec. 28 (1966) 22
[21] TAEUSCH, H. W., M. HEITNER, M. E. AVERY: Accelerated lung maturation and increased survival in premature rabbits treated with hydrocortisone, Amer. Rev. Resp. Dis. 105 (1972) 971
[22] TAEUSCH, H. W., S. H. CARSON, N. S. WANG, M. E. AVERY: Heroin induction of lung maturation and growth retardation in fetal rabbits. J. Pediatrics 82 (1973) 869
[23] WANG, N. S., R. V. KOTAS, M. E. AVERY, W. M. THURLBECK: Accelerated appearance of osmiophilic bodies in fetal lungs following steroid injection. J. Appl. Physiol. 30 (1971) 362
[24] YOON, J. J., R. G. HARPER: Observations on the relationship between duration of rupture of the membranes and the development of RDS. Pediatrics 52 (1973) 161

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